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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.			FRONDA, CHRISTIAN L	
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ALEXANDRIA, VA 22314			PAPER NUMBER	

1652

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/023,889

Applicant(s)

CANFIELD, WILLIAM M.

Examiner

Christian L Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-65 is/are pending in the application.
- 4a) Of the above claim(s) 20-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☒ Claim(s) 7, 14 and 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/02; 3, 7, 9, 12/03; 10/04</u> | 6) <input checked="" type="checkbox"/> Other: <u>CRF form</u> |

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-19, in the **RESPONSE TO RESTRICTION REQUIREMENT** dated 07/22/2004 is acknowledged. The traversal is on the grounds that there would be no serious burden to search all of the inventions of Groups I-V. This is not found persuasive for the reasons stated in the previous Office Action dated 06/23/2004 as supplemented below.

Searching the invention of Groups I-V together in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches which have different limits, boundaries, scope, and subject matter. The searches for each of the inventions of Groups I-V are not coextensive. The inventions of Groups I-V have a separate status in the art as shown by their different classifications. Thus, searching the invention of Groups I-V together would impose a serious search burden.

The requirement is still deemed proper and is therefore made FINAL. Claims 20-66 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Claims 1-19 are under consideration in this Office Action.

3. The paper copy and computer readable form (CRF) of the Sequence Listing filed on 12/21/2001 have been received and have been processed by the Scientific and Technical Information Center (STIC).

Claim Objections

4. Claims 7, 14, and 19 are objected to because of the following informalities:

Claim 7 recites the abbreviation "GlcNAc" in "GlcNAc- phosphotransferase", and claim 14 recites "GlcNAcase" in "phosphodiester α -GlcNAcase". It is suggested that the first time an abbreviation is used in a claim, that the abbreviated term be written out in full, followed by its abbreviation in parenthesis. Appropriate correction is required.

Claim 19 recites the phrase "kifunensine is in present in an amount". It is suggested that the phrase be written as "kifunensine is present in an amount" in order to clarify that the inhibitor is present in the recited concentration range.

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Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line, 1 the phrase "high mannose glycoprotein" renders the claim vague and indefinite because the specification does not define this phrase, but instead defines "high mannose oligosaccharides" as containing only core N-acetylglucosamine (GlcNAc) and mannose moieties. The metes and bounds of the claim are not known to one of ordinary skill in the art at the time the invention was made since it is unclear whether the glycoprotein to be produced has N-linked oligosaccharides having only core GlcNAc and mannose moieties. Claims 2-19 which depend from claim 1 are also rejected because they do not correct the defect of claim 1. For examination purposes and searching of the prior art, the claims are assumed to be directed toward a method for making glycoproteins that have N-linked oligosaccharides having only core GlcNAc and mannose moieties

Claims 11, 12, and 16 are vague and indefinite for reciting the phrase "hybridizes under stringent conditions" since the specification does not define what conditions constitute "stringent" and the claims do not recite the specific hybridization conditions, e.g. wash in 0.1X SSC at a temperature of 68°C. One of ordinary skill in the art at the time the invention was made cannot determine the metes and bounds of the claim since what is considered "stringent" varies widely depending on the situation as well as the person making the determination. Furthermore, it is unclear how similar or homologous any polynucleotide can be to the complements of SEQ ID Nos: 1, 3, 6, or 17 in order to be included within the scope of these claims. For examination purposes and searching of the prior art, the claims are assumed to encompass polynucleotides that have 90% identity to SEQ ID NOS: 1, 3, 6, or 17.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is a genus claim that encompasses methods for making any glycoprotein of any amino acid sequence and structure; where the glycoprotein contains any type of oligosaccharide side chain having any type of mannose structure, and where any mammalian cell containing a polynucleotide encoding the glycoprotein is cultured in any lectin of any amino acid sequence and structure.

The scope of the claims includes many glycoproteins to be produced, where the glycoproteins have many different oligosaccharide side chains and mannose structures; have widely differing structural, chemical, and physical characteristics; and are from many biological sources. In addition, the scope of the claim includes many lectins from many biological sources with widely differing structural, chemical, and physical characteristics. The genus is highly variable because a significant number of structural differences between glycoproteins and their oligosaccharide side chains, and lectins is permitted.

The specification discloses a method for making acid alpha glucosidase (a lysosomal hydrolase) by transforming CHO cell with a cDNA encoding human acid alpha glucosidase, culturing the transformed CHO cell in the presence of ricin to obtain a ricin resistant CHO cell, isolating a ricin resistant CHO cell, and collecting the produced acid alpha glucosidase from the ricin resistant CHO cell, where the produced acid alpha glucosidase has N-linked oligosaccharide side chains containing only core GlcNAc and mannose instead of complex oligosaccharide side chains.

However, the specification does not provide a description of additional lectins, other than ricin, that are used in the claimed method to make any glycoprotein containing any type of oligosaccharide side chain having any type of mannose structure. Furthermore, the specification does not provide a description of additional glycoproteins having any type of oligosaccharide side chain having any type of mannose structure, other than an acid alpha glucosidase having N-linked oligosaccharide side chains containing only core GlcNAc and mannose, which is produced by any lectin resistant mammalian cell.

The disclosed method for making human acid alpha glucosidase is only representative of a genus of methods for making lysosomal hydrolases having N-linked oligosaccharide side

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chains containing only core GlcNAc and mannose by: introducing and transforming a polynucleotide encoding a lysosomal hydrolase into a mammalian cell, culturing the mammalian cell in the presence of ricin, isolating the ricin resistant mammalian cell, culturing the ricin resistant mammalian cell in the presence of deoxymannojirimycin and kifunensine, and collecting the produced lysosomal hydrolases having N-linked oligosaccharide side chains containing only core GlcNAc and mannose.

In view of the above considerations, one of skill in the art would recognize that Applicant has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention.

Claims 2-19 which depend from claim 1 are also rejected because they do not correct the defect of claim 1.

Claim 7 fails to comply with the written description requirement for the following additional reasons. Claim 7 encompasses methods for making any high mannose glycoprotein further comprising contacting the produced glycoprotein with any GlcNAc-phosphotransferase. The claim is a genus claim that is directed toward any GlcNAc-phosphotransferase from any biological source and of any amino acid sequence and structure. The scope of the claims includes many GlcNAc-phosphotransferase enzymes from many biological sources with widely differing structural, chemical, and physical characteristics. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted.

The specification discloses a human GlcNAc-phosphotransferase having an amino acid sequence of SEQ ID NO: 2 and SEQ ID NO: 7. The specification provides a partial amino acid sequence of GlcNAc-phosphotransferase from rat and *Drosophila melanogaster* (SEQ ID NO: 14 and 16, respectively). However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any significant structure and amino acid sequence which would be expected to be common to all members of the genus. Thus, the disclosed GlcNAc-phosphotransferase having an amino acid sequence of SEQ ID NO: 2 and SEQ ID NO: 7 is not representative of the claimed genus since other members of the genus have amino acid sequences and structures that are different from the disclosed GlcNAc-phosphotransferase.

In view of the above considerations, one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by members of the genus. Accordingly, Applicant has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention.

Claim 14 fails to comply with the written description requirement for the following

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additional reasons. Claim 14 encompasses methods for making any high mannose glycoprotein further comprising contacting the produced glycoprotein with any phosphodiester α -GlcNAcase. The claim is a genus claim that is directed toward any phosphodiester α -GlcNAcase from any biological source and of any amino acid sequence and structure. The scope of the claims includes many phosphodiester α -GlcNAcase enzymes from many biological sources with widely differing structural, chemical, and physical characteristics. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted.

The specification discloses a human and murine phosphodiester α -GlcNAcase having an amino acid sequence of SEQ ID NO: 18 and SEQ ID NO: 20, respectively. However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any significant structure and amino acid sequence which would be expected to be common to all members of the genus. Thus, the disclosed human and murine phosphodiester α -GlcNAcase is not representative of the claimed genus since other members of the genus have amino acid sequences and structures that are different from the disclosed phosphodiester α -GlcNAcase.

In view of the above considerations, one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by members of the genus. Accordingly, Applicant has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention.

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-6, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martiniuk et al. (Biochem Biophys Res Commun. 2000 Oct 5;276(3):917-23) in view of the combined teachings of Stanley (Selection of lectin-resistant mutants of animal cells. In Methods in Enzymology, Vol. 96, 1983, pp 157-184), Bijvoet et al. (Hum Mol Genet. 1998 Oct;7(11):1815-24), Fuhrmann et al. (Nature (1984), 307(5953), 755-8), and Elbein et al. (J Biol Chem. 1990 Sep 15;265(26):15599-605).

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Martiniuk et al. teach a method for producing human acid alpha glucosidase (a lysosomal hydrolase) by transforming a polynucleotide encoding human acid alpha glucosidase into Chinese hamster ovary (CHO) cells (a mammalian cell), culturing the transformed CHO cells to express and produce the human acid alpha glucosidase, and collecting and purifying the produced human acid alpha glucosidase by column chromatography (see entire publication and Abstract, especially pp. 918, **MATERIALS AND METHODS**). Martiniuk et al. teach that exposing the recombinant human acid alpha glucosidase (rhGAA) to human GSDII (glycogen storage disease type II) fibroblast cells or patient's lymphocytes or monocytes resulted in uptake of the rhGAA and reversal of the enzymatic defect, while the addition of mannose-6-phosphate in the media blocked uptake of rhGAA in both lymphocytes and monocytes (see pp. 919-920). Martiniuk et al. teach that this rhGAA is ideal for enzyme replacement therapy in GSD II (see Abstract).

Claims 1-6, 18, and 19 differ from the teachings of Martiniuk et al. in that the mammalian cell is cultured in the presence of a lectin to obtain and isolate a lectin resistant mammalian cell, and culturing the lectin resistant mammalian cell in the presence of about 0.1-5.0 mM deoxymannojirimycin and about 0.1-10 ug/ml kifunensine.

Stanley teach culturing Chinese hamster ovary cells (a mammalian cell) in the presence of ricin (a lectin) in a sufficient amount to select and isolate mutant CHO cells that are resistant to ricin, are unable to make complex oligosaccharides on their glycoproteins, and have high mannose type oligosaccharide side chains on their glycoproteins (see entire publication, especially).

Bijvoet et al. teach that enzymes including acid alpha glucosidase that are produced in Chinese hamster ovary cells have carbohydrate side chains with mannose-6-phosphate groups which facilitates the binding and endocytosis of acid alpha glucosidase by cells with cell surface mannose-6-phosphate receptors (see entire publication ,especially p. 1816, left column, 1st full paragraph). Furthermore, Bijvoet et al. teach that CHO cells have been used in the production of other recombinant human lysosomal enzymes that are overexpressed and purified from the culture medium (see p. 1816, left column, lines 5-8).

Fuhrmann et al. teach that deoxymannojirimycin in a concentration of 1mM inhibits mannosidase IA/B activities and blocks the conversion of high mannose oligosaccharides to complex oligosaccharides on IgM and IgD during their biosynthesis in hybridoma cells (see entire publication, especially p. 757, left column, 1st full paragraph to p.758 including Figure 4).

The 1mM concentration of deoxymannojirimycin falls within the concentration range recited in claim 18.

Elbein et al. teach that kifunensine in a concentration of 1 ug/ml or higher inhibits

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mannosidase I and causes a complete shift in the structure of N-linked oligosaccharides from complex chains to high mannose ($\text{Man}_9(\text{GlcNAc})_2$) structures (see entire publication, especially p. 15602 including Table 1 to p.15605); and that kifunensine in combination with deoxymannojirimycin, the formation of complex oligosaccharide chains was almost completely inhibited (see p. 15602, right column, 1st full paragraph).

The 1 ug/ml concentration of kifunensine falls within the concentration range recited in claim 19.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Martiniuk et al. such that the CHO cells transformed to express and produce human acid alpha glucosidase are cultured in a sufficient amount of ricin to select and isolate mutant CHO cells that are resistant to ricin as taught by Bijvoet et al., and then the mutant CHO cells are cultured in the presence of 1mM deoxymannojirimycin and 1 ug/ml kifunensine to inhibit glycosylation of the produced human acid alpha glucosidase as taught by Fuhrmann et al. and Elbein et al., respectively.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to have a beneficial method that produces an acid alpha glucosidase for enzyme replacement therapy, where the acid alpha glucosidase has high mannose type oligosaccharide side chains facilitating the binding and endocytosis of acid alpha glucosidase by cells with cell surface mannose-6-phosphate receptors. Stanley teach that mutant CHO cells that are resistant to ricin are unable to make complex oligosaccharides on their glycoproteins, and have high mannose type oligosaccharide side chains on their glycoproteins. Bijvoet et al. teach acid alpha glucosidase that is produced in Chinese hamster ovary cells have carbohydrate side chains with mannose-6-phosphate groups which facilitates the binding and endocytosis of acid alpha glucosidase by cells with cell surface mannose-6-phosphate receptors. The teachings of Fuhrmann et al. and Elbein et al. enable one of ordinary skill in the art to recognize that the concentration of deoxymannojirimycin and kifunensine would affect the formation of complex oligosaccharides. Taken together, the resulting acid alpha glucosidase would have high mannose type oligosaccharide side chains which can then be used in enzyme replacement therapy to treat glycogen storage disease type II as taught by Martiniuk et al.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success because Bijvoet et al. teach that CHO cells have been used in the production of other recombinant human lysosomal enzymes that are overexpressed and purified from the culture medium and that Stanley teach the successful culturing of CHO cells in the presence of ricin in a sufficient amount to select and isolate mutant CHO cells that are resistant to ricin.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly prima facie obvious.

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11. Claims 7, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martiniuk et al. in view of the combined teachings of Stanley, Bijvoet et al., Fuhrmann et al., and Elbein et al. as applied to claims 1-6, 18, and 19 above, and further in view of Glickman et al. (J Cell Biol. 1993 Oct;123(1):99-108).

The modified method of Martiniuk et al. includes all the limitations recited in claims 1-6, 18, and 19 except for contacting the glycoprotein with a GlcNAc-phosphotransferase and alpha phosphodiester GlcNAcase.

Glickman et al. teach that N-linked oligosaccharides of lysosomal enzymes are modified by the concerted action of UDP-GlcNAc: lysosomal enzyme N-acetyl-glucosamine-1-phosphotransferase (GlcNAc-phosphotransferase) and N-acetylglucosamine-1-phosphate-N-acetylglucosaminidase (phosphodiester alpha GlcNAcase) to generate an exposed mannose-6-phosphate moiety (see entire publication, especially p. 99, left column, 1st paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the modified method of Martiniuk et al. such that the produced acid alpha glucosidase is contacted with GlcNAc-phosphotransferase and the acid alpha glucosidase is purified, or the acid alpha glucosidase is then contacted with phosphodiester alpha GlcNAcase to produce an acid alpha glucosidase that has exposed mannose-6-phosphate residues as taught by Glickman et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this so in order to generate exposed mannose-6-phosphate residues on the produced acid alpha glucosidase, thus facilitating uptake of the acid alpha glucosidase into cells with cell surface mannose-6-phosphate receptors as taught by Bijvoet et al. for use in enzyme replacement therapy.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly prima facie obvious.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

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harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/023,890 in view of the combined teachings of prior art references of Martiniuk et al., Fuhrmann et al., and Elbein et al.

This is a provisional obviousness-type double patenting rejection.

Claims 1-17 of copending application 10/023,890 recite a method for producing a glycoprotein with reduced complex carbohydrates which has method steps that are identical to the method steps of claims 1-17 of the instant application except for the addition of a further step of culturing the lectin resistant mammalian cell in the presence of deoxymannojirimycin and kifunensine in an amount and time to inhibit glycosylation of the glycoprotein.

The teachings of Martiniuk et al., Fuhrmann et al., and Elbein et al. have been stated above.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of claims 1-17 of copending application 10/023,890 such that the lectin resistant mammalian cell is cultured in the presence of deoxymannojirimycin and kifunensine in an amount and time to inhibit glycosylation of the glycoprotein.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to have a beneficial method that produces glycoproteins having high mannose oligosaccharides which are used in enzyme replacement therapy as taught by Martiniuk et al., where the mannosidase inhibitors, deoxymannojirimycin and kifunensine, block the conversion of high mannose oligosaccharides to complex oligosaccharides as taught by Fuhrmann et al. Elbein et al. Although, the preamble of claim 1 of copending application 10/023,890 differs from the preamble of claim 1 of the instant application, the modified method

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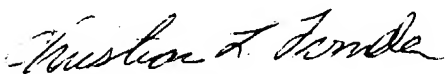
stated above which includes the step of culturing the lectin resistant mammalian cell in the presence of deoxymannojirimycin and kifunensine would result in the production of a glycoprotein having high mannose oligosaccharides, and thus meet the requirement of the preamble of claim 1 of the instant application.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Christian L. Fronda
Art Unit 1652